IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Turner, Sharon L.
Avi J. ASHKENAZI, et al.	)	Art Unit: 1647
Application Serial No. 10/017,191	)	Confirmation No: 6712
Filed: October 24, 2001	)	Attorney's Docket No. 39780-2630 P1C62
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	)	**Customer No. 35489**

DECLARATION OF NAPOLEONE FERRARA, Ph.D., AUDREY GODDARD, Ph.D., PAUL J. GODOWSKI, Ph.D., AUSTIN GURNEY, Ph.D., AND WILLIAM I. WOOD, Ph.D. UNDER 37 C.F.R. §1.131

MAIL STOP AMENDMENT
Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

We, Napoleone Ferrara, Ph.D., Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., Austin Gurney, Ph.D., and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application.

2. We have read and understood the claims pending in this application, and are aware that the claims have been rejected as anticipated by Ford *et al.,* U.S. Patent No. 6,392,018, filed February 12, 1999 and issued May 21, 2002.

3. We conceived and reduced to practice the invention claimed in the above-identified application in the United States prior to February 12, 1999.

4. At the time the present invention was made, one of the inventors, Napoleone Ferrara, Ph.D., was, as still is, responsible for overseeing the testing of novel polypeptides, including the polypeptide designated PRO320, in endothelial cell proliferation assay (Assay #9, Example 109). This assay is used to find agents that are capable of inhibiting proliferation of endothelial cells.

5. In this assay, bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum 12-14 passages) were plated on 96 well plates at a density of 500 CELLS/WELL per 100 L in low glucose DMEM, 10% calf serum. 2 mM glutamine, lx pen/strept and fungizone, supplemented with 3 ng/mL VEGF. Controls were plated the same way but some did not include VEGF. A test sample of the PRO polypeptide of interest was added in a 100 111 volume for a 200 UL FINAL VOLUME. Cells were incubated for 6-7 days at 37°C. The media was aspirated and the cells washed lx with PBS. An acid phosphatase reaction mixture (100 YL, 0. IM sodium acetate, pH 5.5,0.1 % TRITON-100,10 mM p-nitrophenyl phosphate) was added. After incubation for 2 hours at 37°C, the reaction was stopped by addition of 10 JAL IN NaOH. OD was measured on microtiter plate reader at 405 nm. Controls were no cells, cells alone, cells + FGF (5 NG/ML), cells + VEGF (3 NG/ML), cells + VEGF (3 ng/ml) + TGF-ß (1 ng/ml), and cells + VEGF (3ng/mL) + LIF (5 NG/ML). (TGF-P at a I ng/ml concentration is known to block 70-90% of VEGF stimulated cell proliferation.) The results were assessed by calculating the percentage inhibition of VEGF (3 ng/ml) stimulated cells proliferation, determined by measuring acid phosphatase activity at OD405 NM. (1) relative to cells without stimulation, and (2) relative to the reference TGF-ß inhibition of VEGF stimulated activity. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis.

6. Copies of pages from laboratory notebook showing the positive results for the PRO320 polypeptide (SEQ ID NO:140), identified by Pin number P288-1, in Assay #9 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained prior to February 12, 1999.

7. Exhibit A clearly shows that the polypeptide designated PRO320 was tested, and its ability to inhibit the proliferation of endothelial cells was determined prior to February 12, 1999.

8. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Napoleone Ferrara	Date
Audrey Goddard	Date
Paul J. Godowski	Date
Austin Gurney	Date
William I. Wood	Date

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11/29/04 3:21 PM (39780.2630)

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Genentech, Inc.
Attn: Ginger R. Dreger
1 DNA Way
So. San Francisco, CA 94080-4990

Deposited on Behalf of: Genentech, Inc.

Identification Reference by Depositor:	**ATCC Designation**
pRK5-based plasmid DNA48296-1292	209668
pRK5-based plasmid DNA48336-1309	209669
pRK5-based plasmid DNA32284-1307	209670

The deposits were accompanied by: ___ a scientific description _ a proposed taxonomic description indicated above. The deposits were received March 11, 1998 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X. We will not inform you of requests for the strains.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested April 9, 1998. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrator, Patent Depository

Date: April 22, 1998

Assay, Results,

Project No.

Book No. 1351

m Page No. 22

Primary Assay Result												
Assay ID	ASY9											
Assay Name	Endothelial cell growth inhibition											
Date Assayed	1/9/99											
Date Read	1/14/99											
Notebook Num	24961-28											
	1	2	3	4	5	6	7	8	9	10	11	12
	VEGF			+ TOPO			+ LIF			VEGF		
	PIN282-1			PIN283-1			PIN284-1			PIN285-1		
	PIN286-1			PIN287-1			PIN288-1			PIN289-1		
	ROF			Cells Only			Cells Only			No Cells		
A	1.436	1.485	1.448	0.911	0.919	0.209	1.691	1.46	1.582	1.5	1.497	1.564
B	1.676	1.778	1.938	0.741	0.81	0.988	1.048	1.097	1.099	0.77	0.792	0.797
C	1.092	1.201	1.026	0.572	0.571	0.586	1.028	1.062	1.054	1.301	1.436	1.304
D	0.96	1.195	0.997	0.559	0.48	0.561	1.257	1.288	1.313	1.276	1.426	1.498
E	0.785	0.672	0.6	0.696	0.857	0.781	1.03	0.837	0.947	0.905	0.829	0.978
F	1.313	1.508	1.36	1.069	1.397	1.39	1.448	1.4	1.31	0.384	0.42	0.845
G	1.017	1.472	1.206	1.338	1.228	1.376	1.497	1.507	1.391	0.196	0.227	0.41
H	1.189	1.557	1.904	0.921	0.848	0.896	0.63	0.784	0.865	0.076	0.078	0.075

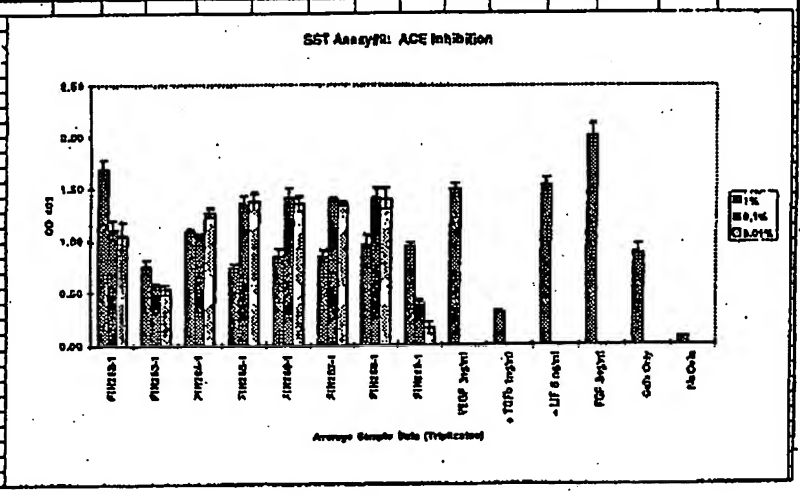
Controls	N1	N2	N3	N4	N5	N6	Average	STDEV
VEGF 3ng/ml	1.44	1.49	1.43	1.50	1.30	1.55	1.46	0.05
+ TOPO 1ng/ml	0.81	0.82	0.81				0.81	0.01
+ LIF 3 ng/ml	1.53	1.46	1.58				1.52	0.06
FGF 3ng/ml	2.18	1.98	1.90				2.00	0.12
Cells Only	0.82	0.73	0.87	0.92	0.95	0.90	0.87	0.08
No Cells	0.08	0.07	0.08				0.07	0.00

	Sample ID	N1	N2	N3	1% Average	1% STDEV	0.1% N1	0.1% N2	0.1% N3	0.1% Average	0.1% STDEV	0.01% N1	0.01% N2	0.01% N3	0.01% Average	0.01% STDEV	>0.7 Fold Positive	Verified	Comments
1	PIN283-1	1.09	1.13	1.10	1.10	0.02	0.73	0.81	0.69	0.74	0.06	0.65	0.80	0.67	0.71	0.08			
2	PIN283-1	0.50	0.54	0.48	0.50	0.01	0.38	0.38	0.40	0.39	0.01	0.38	0.32	0.38	0.36	0.03	Positive		
3	PIN284-1	0.70	0.74	0.74	0.73	0.02	0.68	0.71	0.71	0.70	0.01	0.84	0.89	0.88	0.85	0.03			
4	PIN285-1	0.59	0.48	0.48	0.48	0.02	0.87	0.98	0.88	0.91	0.06	0.89	0.98	0.94	0.92	0.05	Positive		
5	PIN286-1	0.38	0.59	0.60	0.57	0.04	0.88	1.01	0.93	0.94	0.07	0.88	0.88	0.88	0.88	0.00	Positive		
6	PIN287-1	0.60	0.58	0.59	0.57	0.04	0.92	0.94	0.93	0.93	0.01	0.89	0.90	0.92	0.91	0.01	Positive		
7	PIN288-1	0.71	0.56	0.54	0.63	0.07	1.00	0.84	0.88	0.84	0.06	1.01	0.97	0.93	0.94	0.07	Positive		
8	PIN289-1	0.61	0.62	0.65	0.63	0.02	0.28	0.28	0.23	0.26	0.03	0.09	0.15	0.07	0.11	0.04	Positive		

Verify Positive Hits with by typing TRUE or FALSE

Averages	1%	0.1%	0.01%
PIN282-1	1.69	1.11	1.05
PIN283-1	0.75	0.58	0.58
PIN284-1	1.08	1.05	1.27
PIN285-1	0.74	1.35	1.57
PIN286-1	0.65	1.40	1.54
PIN287-1	0.84	1.39	1.55
PIN288-1	0.84	1.40	1.40
PIN289-1	0.94	0.38	0.18
VEGF 3ng/ml	1.49		
+ TOPO 1ng/ml	0.81		
+ LIF 3 ng/ml	1.52		
FGF 3ng/ml	2.00		
Cells Only	0.87		
No Cells	0.07		

STDEV	1%	0.1%	0.01%
PIN282-1	0.08	0.09	0.13
PIN283-1	0.06	0.01	0.05
PIN284-1	0.05	0.02	0.04
PIN285-1	0.03	0.03	0.05
PIN286-1	0.09	0.10	0.07
PIN287-1	0.09	0.01	0.02
PIN288-1	0.11	0.03	0.10
PIN289-1	0.04	0.04	0.08
VEGF 3ng/ml	0.05		
+ TOPO 1ng/ml	0.01		
+ LIF 3 ng/ml	0.06		
FGF 3ng/ml	0.12		
Cells Only	0.04		
No Cells	0.00		



To Page No. 24

nessed & Understood by me. | Date | Invented by | Date